REMARKS

Claims 1-8, 10, 11, 13-14, 16, 20 and 21 are pending. In the instant amendments, claims 7, 10-11, 13 and 15 have been canceled without prejudice. Claims 1-4, 6, 14, 16 and 20 have been amended. Upon entry of the claim amendments, claims 1-6, 8, 14, 16 and 20-21 will be pending and under consideration. Applicants reserve the right to file one or more continuation or divisional applications to any canceled subject matter.

Amendments to the Claims

Claims 1-4 have been amended to recite a "physiologically acceptable" salt of the compound of formula (I). Support for this amendment is found, for example, at page 8, line 19.

Claims 1 and 3 have also been amended to recite "p is 2."

Claim 6 has been amended to recite "one or more pharmaceutically acceptable excipients" as previously recited in canceled claim 7.

Claim 14 has been amended to recite the diseases or disorders, "asthma," "allergic rhinitis" and "lung granuloma." Support for these claims is found, for example, in original claims 14-15.

Claim 16 has been amended to depend from claim 14.

Claim 20 has been amended to depend from claim 7.

These amendments are fully supported by the specification and claims as filed. No new matter is added by the amendments. Entry of the above amendments is respectively requested.

Information Disclosure Statement

The Examiner points out that only the first page of reference C09 was submitted. (Office Action, page 3). Applicants submit herewith for the Examiner's consideration a complete copy of reference C09, and respectfully request that the Examiner acknowledge that the reference has been considered.

Claim Objections

The Examiner has objected to claims 1, 3, 6-8, 10-11, 13-16 and 20-21 as allegedly containing non-elected subject matter because the variable "p" should be "2" in the elected group. (Office Action, page 3). As mentioned above, claims 1 and 3 have also been

amended to recite "p is 2." Upon entry of the claim amendments, claims 6, 8, 13-16 and 20-21, which depend from claim 1, do not contain non-elected subject matter. Therefore, Applicants respectfully request that the claim objections be withdrawn.

Claim Rejections under 35 U.S.C. § 112

Claims 10, 11, 13-16 and 21 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. (Office Action, page 3). Specifically, the Examiner alleges that, while the claims are enabled for the treatment of granulomas, the specification "does not reasonably provide enablement for the treatment of any other disorder." (*Id.*). Applicants respectfully disagree.

Factors to be considered in determining whether a disclosure meets the enablement requirement are set forth in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir 1988). They include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability in the art, (4) the presence or absence of working examples, (5) the amount of guidance presented, (6) the breadth of the claims, (7) the quantity of experimentation necessary, and (8) the level of skill in the art. The initial burden is on the Office to provide evidence of non-enablement for each of these factors. *See In re Wands*, 8 U.S.P.Q.2d at 1404; *see also* MPEP §§ 2164.01(a); 2164.04.

Claims 10, 11, 13 and 15 are canceled. Claim 14 has been amended to recite the following specific diseases or disorders associated with the CCR3 receptor: asthma, alleric rhinitis and lung granuloma. As mentioned in Applicants' response to the Office Action dated August 19, 2008, the instant specification teaches that compounds that antagonize CCR3 are useful in treating the specific diseases and disorders of claim 14. (*See* pages 1-3). Furthermore, as will be demonstrated below, one of ordinary skill in the art at the time of the invention would have recognized a connection between antagonism of the CCR3 receptor and the treatment of these specific diseases and disorders. Therefore, amended claim 14 is enabled by the instant specification.

First, Applicants point out that the Examiner previously acknowledged that the instant claims were enabled for the treatment of asthma and granulomas. (Office Action dated August 19, 2008, page 3). Therefore, Applicants request that the rejection of claim 14 be withdrawn to the extent that it recites the treatment of asthma and lung granuloma.

With regard to allergic rhinitis, Applicants point out that it was well known at the time of the invention that allergic rhinitis and asthma are closely related diseases. *See, e.g.,*

Corren, J., "Allergic rhinitis and asthma: How important the link?," *J Allergy Clin Immunol.*, Vol. 99, pp. S781 -86 (1997) (copy provided with supplement Information Disclosure Statement filed herewith). Corren teaches that "practicing physicians and clinical investigators have long noted a relation between allergic rhinitis and bronchial asthma." (Corren, page S781). Indeed, data from epidemiologic studies show that as many as 78% of patients with asthma experience the symptoms of allergic rhinitis. (*Id.*). Furthermore, Corren teaches that as many as 19 – 38 % of patients with allergic rhinitis may have asthma, as compared to the 3 – 5 % prevelance of asthma in the general population. (*Id.*). Corren also teaches that a study demonstrating that the symptoms of asthma were "virtually eliminated" when corticosteroids for the treatment of allergic rhinitis were administered to patients having asthma. (Corren, page S782). Therefore, based on the teachings of Corren, one of ordinary skill at the art would have expected that a therapeutic agent for the treatment of asthma would be effective in treating allergic rhinitis. And, Applicants point out that the Patent Office has acknowledged that CCR3 was known at the time of the invention to be associated with asthma. (Office Action dated August 19, 2008, page 3). Thus, because the instant claims are enabled for the treatment of asthma, they should be enabled for the treatment of allergic rhinitis.

As further evidence of the link between allergic rhinitis and CCR3, Applicants direct the Examiner's attention to Terada *et al.*, "Biochemical properties of eosinophils and their preferential accumulation mechanism in nasal allergy," *J Allergy Clin Immunol.*, 94: 629-42 (1994) ("Terada," copy provided with supplement Information Disclosure Statement filed herewith). Terada teaches that eosinophil cells are "strong contributors to the onset of the late phase response associated with nasal swelling and hyperreactivity to histamine"—symptoms commonly associated with allergic rhinitis. (Terada, page 629). Terada further discloses the results of a *clinical study* which demonstrates that eosinophils accumulate in the nasal fluid when *human* participants are subjected to an allergen that produces an allergic response. (Terada, page 630). From these results, the authors conclude that a "close relationship exists" between the nasal symptoms of allergic rhinitis and the increase in eosinophils. (Terada, page 634). Terada further teaches that a known approach for controlling eosinophil accumulation is to "control the eosinophil chemoattractant production and its release." (Terada, page 639). And, as taught by the instant specification, the compounds of the instant claims are antagonists of the eosinophil chemoattractant CCR3. Therefore, one of ordinary skill in the art would have expected that the compounds of the

instant claims would be useful in the treatment of allergic rhinitis in view of the teachings of instant specification and the art available at the time of the invention (*i.e.*, Terada). Therefore, instant claim 14 is enabled, to the extent that it recites the treatment of allergic rhinitis. In view of the remarks presented above, Applicants respectfully request that the rejection of claim 14 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

The fee for a Request for Continued Examination will be paid via EFS Web. Pursuant to 37 C.F.R. § 1.136(a)(3), the Commissioner is authorized to charge any additional fees, or credit any overpayment, to Jones Day, U.S. Deposit Account No. 503013 (referencing 191354-999004).

If the Examiner believes it would be useful to advance prosecution, the Examiner is invited to telephone the undersigned at (858) 314-1200.

Respectfully submitted,

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